PC25146

CLAIMS

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What is claimed is:

1. A compound of Formula (I)

wherein

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X is carbon and Y is nitrogen or X is nitrogen and Y is carbon;

R¹ is hydrogen, (C₁-C₆)alkyl, halogen, or cyano;

 R^2 and R^3 are each independently $(CH_2)_n$ -aryl or $(CH_2)_n$ -heteroaryl, where n is 0, 1 or 2, and where said aryl and said heteroaryl moieties are optionally substituted with one or more substituents;

L is -C(O)- or -C(R⁴)(OR⁵)-, where R⁴ is hydrogen or (C₁-C₆)alkyl and R⁵ is hydrogen, (C₁-C₆)alkyl, or taken together with R⁸ or R⁹ is -CH₂CH₂- or -CH₂C(O)-;

 R^6 and R^7 are each independently hydrogen or (C₁-C₆)alkyl, or R^6 and R^7 taken together form a partially or fully saturated carbocyclic ring; and

 R^8 and R^9 are each independently hydrogen, (C_1-C_6) alkyl, $-C(O)(CH_2)_mR^{10}$, $-SO_2(CH_2)_nR^{10}$, or $-(CH_2)_pR^{10}$, where m and n are 0, 1, or 2, p is 0, 1, 2 or 3, and R^{10} is selected from the group consisting of (C_1-C_8) alkyl, a partially or fully saturated cycloalkyl, aryl, heteroaryl, and a partially or fully saturated heterocycle, where said (C_1-C_8) alkyl, said cycloalkyl, said aryl, said heteroaryl and said heterocycle are optionally substituted with one or more substituents; or

R⁸ and R⁹ taken together form a partially or fully saturated, 4- to 8-membered heterocyclic ring containing 1 to 3 heteroatoms and optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, a prodrug of said compound or said salt, or a solvate or hydrate of said compound, said salt or said prodrug.

2. The compound of Claim 1, wherein said compound of Formula (I) is a compound of Formula (IA)

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wherein

R¹ is hydrogen or (C₁-C₆)alkyl;

 R^2 and R^3 are each independently -(CH_2)_n-aryl or -(CH_2)_n-heteroaryl, where n is 0, 1 or 2, and where said aryl and said heteroaryl moieties are each optionally substituted with one to three substituents; and

 R^6 and R^7 are each independently hydrogen or (C₁-C₆)alkyl, or R^6 and R^7 taken together form a partially or fully saturated carbocyclic ring; and

R⁸ and R⁹ taken together form a partially or fully saturated, 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms and optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, a prodrug of said compound or said salt, or a solvate or hydrate of said compound, said salt or said prodrug.

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- 3. The compound of Claim 2 selected from the group consisting of
- 1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-piperidin-1-yl-ethanone;
- 1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-morpholin-4-yl-ethanone;
- 1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-[4-(1-methyl-1H-pyrrole-2-carbonyl)-piperazin-1-yl]-ethanone;
- 1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropanecarbonyl)-piperazin-1-yl]-ethanone;
 - N-(1-{2-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-oxo-ethyl}-piperidin-4-yl)-2,2,2-trifluoro-acetamide;
 - 1-[5-(4-chloro-phenyl)-1-(2-fluoro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-morpholin-4-yl-ethanone;
 - 1-[5-(4-chloro-phenyl)-1-(2-fluoro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-piperidin-1-yl-ethanone;
 - 1-[5-(4-chloro-phenyl)-1-(2-fluoro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-(4-trifluoroacetyl-piperazin-1-yl)-ethanone;
- 1-[1-(2-chloro-phenyl)-5-(4-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-pyrrolidin-1-yl-ethanone;
 - 1-[1-(2-chloro-phenyl)-5-(4-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-[1,4]oxazepan-4-yl-ethanone; and
 - 1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-(1-oxa-8-aza-spiro[4.5]dec-8-yl)-ethanone;
- a pharmaceutically acceptable salt thereof or a solvate or hydrate of said compound or said salt.
 - 4. The compound of Claim 1, wherein said compound of Formula(I) is a compound of Formula (IB)

$$\begin{array}{c|c}
R^{1} & OR^{5} & R^{8} \\
R^{1} & N & R^{6} & R^{7} \\
R^{2} & N & R^{6} & R^{7}
\end{array}$$
(IB)

wherein

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R¹ is hydrogen or (C₁-C₆)alkyl;

 R^2 and R^3 are each independently -(CH₂)_n-aryl or -(CH₂)_n-heteroaryl, where n is 0, 1 or 2, and where said aryl and said heteroaryl moieties are each optionally substituted with one to three substituents;

R⁴ is hydrogen or (C₁-C₆)alkyl;

R⁵ is hydrogen or (C₁-C₆)alkyl;

R⁶ and R⁷ are each independently hydrogen or (C₁-C₆)alkyl, or R⁶ and R⁷ taken together form a partially or fully saturated carbocyclic ring; and

 R^8 and R^9 are each independently hydrogen, (C_1-C_6) alkyl, $-C(O)(CH_2)_mR^{10}$, $-SO_2(CH_2)_nR^{10}$, or $-(CH_2)_pR^{10}$, where m and n are 0, 1, or 2, p is 0, 1, 2 or 3, and R^{10} is selected from the group consisting of (C_1-C_8) alkyl, a partially or fully saturated cycloalkyl, aryl, heteroaryl, and a partially or fully saturated heterocycle, where said (C_1-C_8) alkyl, said cycloalkyl, said aryl, said heteroaryl and said heterocycle are optionally substituted with one or more substituents, or

R⁸ and R⁹ taken together form a partially or fully saturated, 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms and optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, a prodrug of said compound or said salt, or a solvate or hydrate of said compound, said salt or said prodrug.

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5. The compound of Claim 4 selected from the group consisting of

2-(benzyl-isopropyl-amino)-1-[1-(2-chloro-phenyl)-5-(4-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-ethanol;

1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-(3,5-dimethyl-piperidin-1-yl)-ethanol;

1-{2-[1-(2-chloro-phenyl)-5-(4-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-hydroxy-ethyl}-4-isopropylamino-piperidine-4-carboxylic acid amide;

1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-(3,3-dimethyl-piperidin-1-yl)-ethanol;

1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-piperidin-1-yl-ethanol; and

1-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-2-morpholin-4-yl-ethanol;

a pharmaceutically acceptable salt thereof or a solvate or hydrate of said compound or said salt.

6. The compound of Claim 1 wherein said compound of Formula (I) is a compound of Formula (IC)

$$R^{1}$$
 R^{2}
 N
 R^{6}
 R^{7}
 R^{3}
(IC)

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wherein

R¹ is hydrogen or (C₁-C₆)alkyl;

 R^2 and R^3 are each independently -(CH₂)_n-aryl or -(CH₂)_n-heteroaryl, where n is 0, 1 or 2, and where said aryl and said heteroaryl moieties are each optionally substituted with one to three substituents;

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R⁶ and R⁷ are each independently hydrogen or (C₁-C₆)alkyl, or R⁶ and R⁷ taken together form a partially or fully saturated carbocyclic ring; and

 R^9 is hydrogen, (C_1-C_6) alkyl, $-C(O)(CH_2)_mR^{10}$, $-SO_2(CH_2)_nR^{10}$, or $-(CH_2)_pR^{10}$, where m and n are 0, 1, or 2, p is 0, 1, 2 or 3, and R^{10} is selected from the group consisting of (C_1-C_8) alkyl, a partially or fully saturated cycloalkyl, aryl, heteroaryl, and a partially or fully saturated heterocycle, where said (C_1-C_8) alkyl, said cycloalkyl, said aryl, said heteroaryl and said heterocycle are optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, a prodrug of said compound or said salt, or a solvate or hydrate of said compound, said salt or said prodrug.

- 7. The compound of Claim 6 selected from the group consisting of
- 2-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-4-cyclohexyl-morpholine;
 - 2-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-4-(propane-2-sulfonyl)-morpholine;
 - 2-[5-(4-chloro-phenyl)-1-(2-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-4-(toluene-4-sulfonyl)-morpholine;
 - 1-{2-[1-(2-chloro-phenyl)-5-(4-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-morpholin-4-yl}-2-methyl-propan-1-one;
 - 2-[1-(2-chloro-phenyl)-5-(4-chloro-phenyl)-4-methyl-1H-pyrazol-3-yl]-4-(4-trifluoromethyl-benzyl)-morpholine; and
- a pharmaceutically acceptable salt thereof or a solvate or hydrate of said compound or said salt.
 - 8. The compound of Claim 1, wherein said compound of Formula (I) is a compound of Formula (ID)

$$R^1$$
 R^2
 N
 R^3
(ID)

wherein

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R¹ is hydrogen or (C₁-C₆)alkyl;

 R^2 and R^3 are each independently -(CH₂)_n-aryl or -(CH₂)_n-heteroaryl, where n is 0, 1 or 2, and where said aryl and said heteroaryl moieties are each optionally substituted with one to three substituents;

R⁶ and R⁷ are each independently hydrogen or (C₁-C₆)alkyl, or R⁶ and R⁷ taken together form a partially or fully saturated carbocyclic ring; and

R⁸ and R⁹ taken together form a partially or fully saturated, 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms and optionally substituted with one or more substituents;

a pharmaceutically acceptable salt thereof, a prodrug of said compound or said salt, or a solvate or hydrate of said compound, said salt or said prodrug.

9. The compound of Claim 8 selected from the group consisting of

1-[1-(4-chloro-phenyl)-2-(2,4-dichloro-phenyl)-5-methyl-1H-imidazol-4-yl]-2-piperidin-1-yl-ethanone; and

1-[1-(4-chloro-phenyl)-2-(2,4-dichloro-phenyl)-5-methyl-1H-imidazol-4-yl]-2-morpholin-4-yl-ethanone;

a pharmaceutically acceptable salt thereof or a solvate or hydrate of said compound or said salt.

10. The compound of Claim 1, 2, 4, 6, or 8 wherein R^2 is p-chlorophenyl or p-fluorophenyl, and R^3 is 2,4-dichlorophenyl, 2-chlorophenyl or 2-flurorophenyl.

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- 11. A pharmaceutical composition comprising
 - (a) a compound of Claim 1, a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt; and
 - (b) a pharmaceutically acceptable excipient, diluent, or carrier.

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12. The composition of Claim 10 further comprising a nicotine receptor partial agonist, an opioid antagonist, a dopaminergic agent, an attention deficit disorder agent, or an anti-obesity agent.

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13. The composition of Claim 12 wherein said anti-obesity agent is selected from the group consisting of an apo-B/MTP inhibitor, a 11β-hydroxy steroid dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR-4 agonist, a CCK-A agonist, a monoamine reuptake inhibitor, a sympathomimetic agent, a β₃ adrenergic receptor agonist, a dopamine agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT2c receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a ciliary neurotrophic factor, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

- 14. A method for treating a disease, condition or disorder modulated by a cannabinoid receptor antagonist in animals comprising the step of administering to an animal in need of such treatment a therapeutically effective amount of a compound of Claim 1, a pharmaceutically acceptable salt thereof, or a solvate or hydrate of said compound or said salt.
- 15. The method of Claim 14 wherein said cannabinoid receptor is a CB1 receptor.

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- 16. The method of Claim 15 wherein said disease, condition or disorder modulated by a cannabinoid receptor antagonist is selected from the group consisting of weight loss, obesity, bulimia, depression, atypical depression, bipolar disorders, psychoses, schizophrenia, behavioral addictions, suppression of reward-related behaviors, alcoholism, tobacco abuse, memory loss, Alzheimer's disease, dementia of aging, seizure disorders, epilepsy, attention deficit disorder, Parkinson's disease, gastrointestinal disorders, and type II diabetes.
- 17. The method of Claim 15 wherein said disease is obesity, bulimia, attention deficit disorder, alcoholism, or tobacco abuse.
- 18. A method for treating a disease, condition or disorder modulated by a cannabinoid receptor antagonist in animals comprising the step of administering to an animal in need of such treatment two separate pharmaceutical compositions comprising
 - (i) a first composition comprising a compound of Claim 1 and a pharmaceutically acceptable excipient, diluent, or carrier, and

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- (ii) a second composition comprising at least one additional pharmaceutical agent and a pharmaceutically acceptable excipient, diluent, or carrier.
- 19. The method of Claim 18 wherein said at least one additional pharmaceutical agent is a nicotine partial agonist, an opioid antagonist, a dopaminergic agent, an attention deficit disorder agent, or an anti-obesity agent.
- The method of Claim 19 wherein said anti-obesity agent is 20. selected from the group consisting of an apo-B/MTP inhibitor, a 11β-hydroxy steroid dehydrogenase-1 inhibitor, peptide YY₃₋₃₆ or an analog thereof, a MCR-4 agonist, a CCK-A agonist, a monoamine reuptake inhibitor, a sympathomimetic agent, a β₃ adrenergic receptor agonist, a dopamine agonist, a melanocyte-stimulating hormone receptor analog, a 5-HT2c receptor agonist, a melanin concentrating hormone antagonist, leptin, a leptin analog, a leptin receptor agonist, a galanin antagonist, a lipase inhibitor, a bombesin agonist, a neuropeptide-Y receptor antagonist, a thyromimetic agent, dehydroepiandrosterone or analog thereof, a glucocorticoid receptor antagonist, an orexin receptor antagonist, a glucagon-like peptide-1 receptor agonist, a ciliary neurotrophic factor, a human agouti-related protein antagonist, a ghrelin receptor antagonist, a histamine 3 receptor antagonist or inverse agonist, and a neuromedin U receptor agonist.

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- 21. The method of Claim 18 wherein said first composition and said second composition are administered simultaneously.
- 22. The method of Claim 18 wherein said first composition and said second composition are administered sequentially and in any order.

23. The method of Claim 18, 19, 20, 21, or 22 wherein said disease is obesity, bulimia, attention deficit disorder, alcoholism, or tobacco abuse.